UNSYMMETRICAL BOROLE COMPLEXES OF MONOBASIC BIDENTATE BENZOTHIAZOLINES

Taruna Pandey and R. V. Singh*

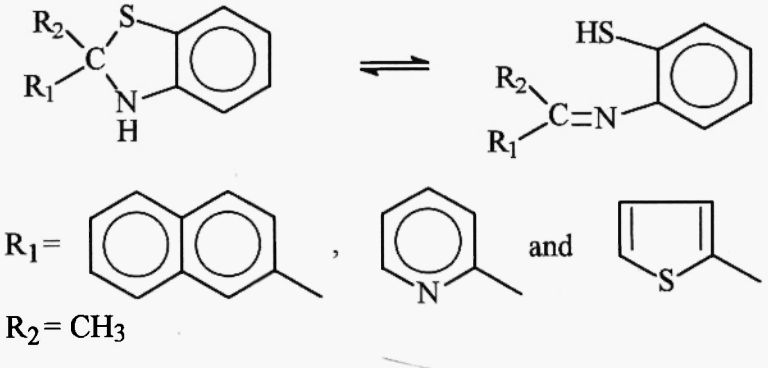
Department of Chemistry, University of Rajasthan, Jaipur – 302004, India

ABSTRACT

The synthetic spectroscopic and biological studies of some unsymmetrical borole complexes derived from heterocyclic ketones and 2-mercaptoaniline have been characterized on the basis of elemental analysis molecular weight determinations and spectral studies including IR, ^{1}H NMR, ^{13}C NMR and ^{11}B NMR. The equimolar reaction between unsymmetrical borole and these benzothiazolines have produced [$B(C_3H_6O_2)$ (N^S)] and [$B(C_4H_8O_2)$ (N^S)] type of boron complexes. The spectroscopic results show that the benzothiazolines behave in a monobasic bidentate fashion rendering the non-metal tetracoordinated. The benzothiazolines and their respective non-metal complexes have been screened for their antifungal and antibacterial properties.

INTRODUCTION

Boron and its compounds have attracted the attention of a large number of chemists mainly because of the tremendous range of structural peculiarities and subtle types of bonding. Boron shows an astonishing number of structural polymorphs. Further, the synthetic flexibility of boron, which has a wide range of applications in various disciplines, has attracted a number of investigators in the field. Arene boronic acids show antiserotonin activity[1]. The toxicity to mice of a number of triarylboranes and their amine complexes has been investigated[2]. Recently, interest has also been sustained in the structural aspects of compounds containing boron – nitrogen bonds[3-7]. Benzothiazolines, which are biologically very active, constitute an important class of nitrogen and sulphur donor ligands[8-9]. The inherent biological potential of sulphur donor ligands prompted us to prepare unsymmetrical borole complexes of benzothiazolines. We report the synthesis, characterization and biological activity of boron complexes with biologically active monobasic bidentate benzothiazolines B_Zt_1H, B_Zt_2H and B_Zt_3H synthesized by the condensation of 2-mercaptoaniline with heterocyclic ketones, [1–(2–naphthenyl)ethanone], [1–(2–pyridinyl)ethanone] and [1–(2–thienyl) ethanone], respectively. The benzothiazolines used can structurally be depicted as follows:



RESULTS AND DISCUSSION

The equimolar reactions of 2-isopropoxy – 4 – methyl – 1, 3, 2 – dioxaborolane [$B(C_3H_6O_2)$ (OPr^i)] and 2–isopropoxy–4–methyl–1,3,2–dioxaborinane with monobasic bidentate benzothiazolines liberated isopropanol azeotropically with benzene.

$$[B(C_3H_6O_2)\ (OPr^i)] + N^{\frown}S\ H \xrightarrow[\text{benzene}]{} [B(C_3H_6O_2)\ (N^{\frown}S)] + Pr^iOH$$

$$[B(C_4H_8O_2)\ (OPr^i)] + N^{\frown}S\ H \xrightarrow[\text{benzene}]{} [B(C_4H_8O_2)\ (N^{\frown}S)] + Pr^iOH$$

(Where, N^S represents the donor set of benzothiazolines)

The resulting coloured solids are soluble in MeOH, DMF and DMSO. The above reactions are quite facile and can be completed in 10–12 hrs. of refluxing. The method used for the preparation and isolation of the resulting complexes give materials of good purity as supported by their analysis. The complexes are monomeric as indicated by the molecular weight determinations. The low molar conductance value (10-14 ohm^{-1} cm^2 mol^{-1}) reveals the non-electrolytic nature of the synthesized complexes.

Electronic Spectra

The electronic spectra of benzothiazolines consist of two bands around 250 and 315 nm, characteristics of benzothiazolines[10]. These may be attributed to the ϕ-ϕ* and π-π* (benzenoid) transitions, respectively[11]. A new band around 400 nm due to n-π* electronic transitions of the azomethine group is observed in the spectra of unsymmetrical borole derivatives. This suggests the formation of azomethine grouping on complexation and subsequent isomerization of the benzothiazolines into the azomethine form.

Infrared Spectra

In the IR spectra of benzothiazolines the absence of υ (SH) at 2600-2500 cm^{-1} and υ (C=N) at 1630-1600 cm^{-1} is a strong evidence for the ring structure[12]. On complexation the band at 3250-3100 cm^{-1} due to NH[13] stretching vibrations of the benzothiazolines disappears and a new band at ~ 1600 cm^{-1} is observed due to υ (C=N) vibrations. The chelation of these benzothiazolines through the azomethine nitrogen and thiolic sulphur further gets support by the appearance of new bands at ca. 1565-1535 cm^{-1} and at 780-760 cm^{-1} in the spectra of complexes due to υ (B←N)[14] and υ (B-S)[15] vibrations, respectively.

^{1}H NMR Spectra

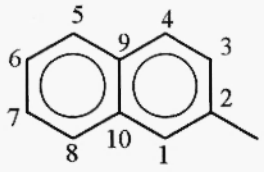
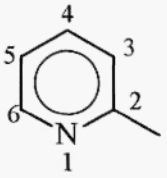
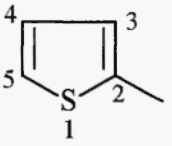
The proton magnetic resonance spectra of benzothiazolines and their corresponding unsymmetrical borole complexes have been recorded in DMSO-d_6 using TMS as the internal standard. The chemical shifts of different protons are given in Table I. The signals of the NH proton at δ5.52 to δ4.32 ppm in benzothiazolines, are found to be absent in their borole complexes confirming the deprotonation of NH group and coordination of boron with nitrogen atom.

Table I: ^{1}H and ^{11}B NMR Spectral Data (δ, ppm/JHz) of Benzothiazolines and their Corresponding Borole Complexes

Compound	-NH	-CH_3	Aromatic Protons*						^{11}B
	(bs)	(s)	1	3	4	5	6	7	
Bzt_1H	5.52	3.42	7.32(s)		7.12-6.96(m)		6.72-6.40(m)		-
$B(C_3H_6O_2)(Bzt_1)$	-	3.59	7.54(s)		7.28-7.04(m)		6.80-6.59(m)		0.72
$B(C_4H_8O_2)(Bzt_1)$	-	3.65	7.67(s)		7.36-7.20(m)		6.88-6.63(m)		1.15
Bzt_2H	5.40	3.36	-	6.40(d) ($7.2Hz$)	6.88(dd) ($7.7Hz$) ($7.2Hz$)	6.36(dd) ($7.7Hz$) (7.4 Hz)	7.28(d) ($7.4Hz$)	-	-
$B(C_3H_6O_2)(Bzt_2)$	-	3.59	-	6.72(d) ($7.1Hz$)	7.04(dd) ($7.8Hz$) ($7.1Hz$)	6.52(dd) ($7.8Hz$) ($7.4Hz$)	7.51(d) ($7.4Hz$)	-	2.21
$B(C_4H_8O_2)(Bzt_2)$	-	3.67	-	6.80(d) ($7.1Hz$)	6.96(dd) ($7.9Hz$) ($7.1Hz$)	6.59(dd) ($7.9Hz$) ($7.5Hz$)	7.62(d) ($7.5Hz$)	-	2.63
Bzt_3H	4.32	+		6.40(d) ($7.3Hz$)	6.80(dd) ($7.3Hz$) ($7.4Hz$)	7.24(d) ($7.4Hz$)	-	-	-
$B(C_3H_6O_2)(Bzt_3)$	-	5.74	-	6.62(d) ($7.4Hz$)	6.96(dd) ($7.4Hz$) ($7.5Hz$)	7.57(d) ($7.5Hz$)	-	-	3.76
$B(C_4H_8O_2)(Bzt_3)$	-	5.82	-	6.73(d) ($7.2Hz$)	6.96(dd) ($7.2Hz$) ($7.3Hz$)	7.64(d) ($7.3Hz$)	-	-	4.02

+ merged with -NH protons.

In Bzt_1H we found two sets of multiplets (3,4,5,8 & 6,7)

The change in the positions of CH_3-C=N protons of the benzothiazolines in the spectra of complexes is a strong evidence of the formation of coordinate linkage between nitrogen and boron.

^{13}C NMR Spectra

The ^{13}C NMR spectra of benzothiazolines and corresponding borole complexes were also recorded in dry DMSO and assigned peak positions are listed in Table II. The shifts in the position of the carbon attached to S and N indicate their coordination with the boron atom.

Table II: ^{13}C NMR Spectral Data*(δ, PPM) of Benzothiazolines and their Corresponding Borole Complexes

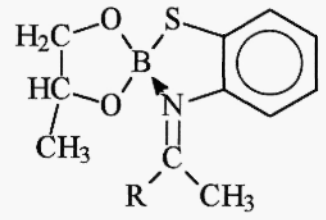
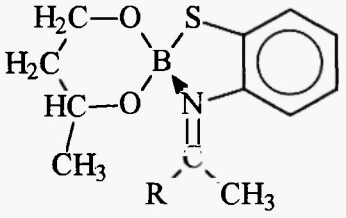
Compound	C-N/C=N	C=S	- CH_3	Aromatic
Bzt_1H	149.68	137.25	14.27	C_1 126.33; C_2 130.18; C_3 125.66; C_4 124.68; C_5 124.54; C_6 123.54; C_7 122.42; C_8 120.73; C_9 119.73; C_{10} 120.68; C_{11} 119.54; C_{12} 117.64; C_{13} 115.68; C_{14} 115.45; C_{15} 113.44
$B(C_3H_6O_2)(Bzt_1)$	162.71	151.40	15.23	C_1 127.68; C_2 131.28; C_3 126.22; C_4 125.05; C_5 124.63; C_6 124.59; C_7 122.67; C_8 121.62; C_9 119.85; C_{10} 120.91; C_{11} 120.12; C_{12} 117.88; C_{13} 116.91; C_{14} 116.02; C_{15} 113.56
$B(C_4H_8O_2)(Bzt_1)$	169.84	156.57	15.47	C_1 127.68; C_2 131.28; C_3 126.22; C_4 125.05; C_5 124.63; C_6 125.12; C_7 123.17; C_8 120.86; C_9 119.82; C_{10} 121.89; C_{11} 119.57; C_{12} 118.20; C_{13} 116.95; C_{14} 115.64; C_{15} 114.15
Bzt_2H	151.24	139.68	13.15	C_2 126.90; C_3 125.70; C_4 125.73; C_5 125.81; C_6 126.51; C_7 125.63; C_8 123.19; C_9 121.80; C_{10} 121.75; C_{11}120.40
$B(C_3H_6O_2)(Bzt_2)$	168.24	150.63	14.17	C_2 127.21; C_3 125.99; C_4 125.91; C_5 125.98; C_6 126.77; C_7 126.23; C_8 123.26; C_9 121.98; C_{10} 122.72; C_{11}121.51
$B(C_4H_8O_2)(Bzt_2)$	172.62	159.73	14.29	C_2 127.32; C_3 125.94; C_4 125.75; C_5 126.37; C_6 126.76; C_7 126.82; C_8 124.02; C_9 122.68; C_{10} 122.56; C_{11} 20.79
Bzt_3H	148.64	134.50	12.34	C_2 130.13; C_3 126.48; C_4 124.24; C_5 125.23; C_6 123.76; C_7 120.82; C_8 115.60; C_9 115.18; C_{10} 113.80
$B(C_3H_6O_2)(Bzt_3)$	165.76	152.42	13.23	C_2 131.01; C_3 126.57; C_4 124.56; C_5 126.12; C_6 123.96; C_7 121.56; C_8 115.77; C_9 116.02; C_{10} 113.98
$B(C_4H_8O_2)(Bzt_3)$	169.82	156.54	13.36	C_2 132.11; C_3 126.76; C_4 124.50; C_5 125.52; C_6 124.13; C_7 120.97; C_8 115.85; C_9 116.15; C_{10} 114.02

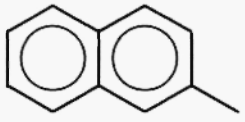
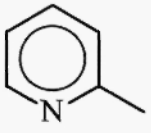
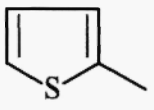
* Assignments were done based on available literature.

^{11}B NMR Spectra

The ^{11}B NMR spectra of benzothiazolines and complexes were recorded in DMSO-d_6 using BF_3 Et_2O as external standard. The ^{11}B NMR spectra give signals in the range δ 0.72–4.02 ppm, indicating the tetracoordinated state[16] of boron in these unsymmetrical borole derivatives.

Thus on the basis of above discussions it is clear that the benzothiazolines by coordinating to boron atom through the thiolo group and azomethine nitrogen behave as monobasic bidentate agents. The spectral evidences also lend support to the proposed coordination in these complexes and the following tentative structures have been proposed for the resulting products:

R =  ,  and 

BIOCIDAL ACTIVITY

The biocidal activities of heterocyclic benzothiazolines and their corresponding unsymmetrical borole complexes against different fungi and bacteria have been recorded in Tables III and IV by the agar plate technique and paper disc plate method[17], respectively.

Table III: Fungicidal Screening Data of Benzothiazolines and their Corresponding Borole Complexes (Average Percentage inhibition after 96 hours)

Compound	Macrophomina phaseolina Conc in ppm			Fusarium oxysporum Conc in ppm		
	50	100	200	50	100	200
$BztH$	28	43	56	40	52	64
Bzt_2H	28	37	52	24	35	58
Bzt_3H	23	31	52	31	35	41
$B(C_3H_6O_2)(Bzt)$	40	61	75	52	61	72
$B(C_3H_6O_2)(Bzt_2)$	42	69	77	53	63	74
$B(C_3H_6O_2)(Bzt_3)$	48	70	79	56	68	78
$B(C_4H_8O_2)(Bzt)$	65	76	82	67	78	83
$B(C_4H_8O_2)(Bzt_2)$	78	84	87	72	79	85
$B(C_4H_8O_2)(Bzt_3)$	80	86	88	82	85	89

Table IV: Bactericidal Screening Data of Benzothiazolines and their Corresponding Borole Complexes

Compound	Diameter of inhibition zone (mm)					
	Pseudomonas cepacicola (-)		Klebsiella aerogenous (-)		Escherichia coli (-)	
	500	1000	500	1000	500	1000
$BztH$	4	7	4	7	5	8
Bzt_2H	4	6	3	5	5	7
Bzt_3H	5	8	4	5	4	8
$B(C_3H_6O_2)(Bzt)$	5	8	6	8	7	9
$B(C_3H_6O_2)(Bzt_2)$	6	8	5	7	6	8
$B(C_3H_6O_2)(Bzt_3)$	7	11	7	7	9	11
$B(C_4H_8O_2)(Bzt)$	9	9	9	10	9	12
$B(C_4H_8O_2)(Bzt_2)$	8	10	8	9	8	10
$B(C_4H_8O_2)(Bzt_3)$	8	12	8	11	10	12

The results showed that the benzothiazolines alone were quite toxic but their activity increased on undergoing complexation. The mechanism of the toxicity of the compounds compared with the parent benzothiazolines may be ascribed to increase lipophilic nature of the central boron atom arising due to chelation.

EXPERIMENTAL

All the glass apparatus with standard quick fit joints was used throughout. Adequate precautions were taken to exclude moisture from the system. The chemicals and solvents used were dried and purified by standard methods.

Table V : Physical Properties of Benzothiazolines

Compound	Colour	M.P(^{0}C)	Analysis % Found(Calcd.)				Mol. Wt.Found(Calcd.)
			C	N	S	H	
BZt_1H	Yellow	88	78.0(77.8)	5.0(4.8)	11.5(11.1)	5.4(5.2)	277(290)
BZt_2H	Yellow	87	72.9(72.3)	13.0(12.6)	14.9(14.2)	5.6(5.4)	214(255)
BZt_3H	Yellow	85	91.2(90.9)	8.8(8.2)	40.5(39.9)	7.0(6.8)	158(180)

Preparation of Benzothiazolines

The benzothiazolines were prepared by the condensation of [1–(2–naphthenyl) ethanone], [1–(2–pyridinyl)ethanone] and [1–(2–thienyl)ethanone] with 2-mercaptoaniline in 1:1 molar ratio in EtOH. The reaction mixture was stirred for 3-4 hours and the solid which separated out was filtered off, recrystallized from EtOH and dried in vacuo. All the products are coloured solids.

Synthesis of Unsymmetrical Borole Complexes

The unsymmetrical monoisopropoxy borane was taken in benzene and an equimolar quantity of the benzothiazolines (BZt_1H, BZt_2H and BZt_3H) was added in it. The reaction mixture was refluxed for 10-12 hrs. and the liberated isopropanol was fractionated azeotropically with benzene. After the completion of the reaction, the excess of the solvent was distilled off and the product was dried in vacuo. It was repeatedly washed with dry cyclohexane and again dried for 3-4 hrs. The complexes were recrystallized from benzene/ether (1/1).

Table VI : Physical Properties of Unsymmetrical Borole Complexes

Compound	Colour and M.P(^{0}C)	Analysis % Found(Calcd.)					Mol.Wt.Found(Calcd.)
		C	N	S	B	H	
$B(C_3H_6O_2)(BZt_1)$	Yellow,98-102	69.8(69.1)	3.8(3.1)	8.8(8.3)	2.9(2.6)	5.5(5.1)	361(380)
$B(C_3H_6O_2)(BZt_2)$	Blakish green,99-104	64.4(63.9)	9.4(8.9)	10.7(10.1)	3.6(3.4)	5.7(5.3)	298(315)
$B(C_3H_6O_2)(BZt_3)$	Greenish yellow,103-106	74.4(74.1)	5.7(5.1)	26.4(26.1)	4.4(4.1)	6.6(6.4)	242(260)
$B(C_4H_8O_2)(BZt_1)$	Yellow,105-108	70.4(69.9)	3.7(3.2)	8.5(8.0)	2.8(2.5)	5.9(5.4)	375(390)
$B(C_4H_8O_2)(BZt_2)$	Blackish green,110-112	65.4(65.2)	8.9(8.1)	10.2(9.8)	3.4(3.1)	6.1(5.8)	312(340)
$B(C_4H_8O_2)(BZt_3)$	Greenish yellow,113-116	75.0(74.8)	5.4(4.8)	25.0(24.8)	4.2(3.9)	7.0(6.7)	256(275)

Analytical Methods and Physical Measurements

Nitrogen and sulphur were estimated by the Kjeldahl's and Messenger's Methods, respectively. Carbon and hydrogen analyses were performed at the Microanalytical Laboratory of the Department. Boron was estimated volumetrically as boric acid[18]. The molecular weights were determined by the Rast-Camphor method. Infrared spectra with KBr optics were obtained using Perkin-Elmer 577 Grating Spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 using TMS as the standard on a Jeol FX 90 Q Spectrometer. ^{11}B spectra were scanned on Bruker WH 90 Spectrometer operating at 64.21 MH_z at 31°C using $BF_3.Et_2O$ as an external standard.

BIOCIDAL SCREENING

The synthesized benzothiazolines and their corresponding unsymmetrical borole complexes were tested for the in vitro growth inhibitory activity against pathogenic fungi, viz. Macrophomina, phaseolina, Fusarium oxysporum and bacteria, viz., Pseudomonas cepacicola, Klebsiella aerogenous and Escherichia coli. Proper temperature, necessary nutrients and growth media free from other microorganisms were employed for the preparation of cultures of fungi and bacteria using aseptic techniques[19].

ACKNOWLEDGEMENT

The authors are thankful to Dr. Neelima, Assistant Professor, Department of Chemistry, University of Rajasthan, Jaipur for helping in preparing the structures.

REFERENCES

1. F. Caujolle, Pham – Huu – Chank and M.C Azum Gelade *Agressologia*, **9** (1968), 457.
2. V.S Zalesov, V.E Kolla, L.M Filatoua and G.A. Yuzhakova, *Nauch. Tr–Perm, Farm Inst.*, (1967), 27.
3. B.M. Mikhailov, G.S. Ter – Sarkisyan, N.N. Govorov and N.A Nikolaeva, *Khim, Elementroorg. Soedin*, (1976), 3; *Chem. Abst.*, **86** (1977), 16721 x.
4. B.M. Mikhailov, G.S. Ter – sarkisyan, N.N. Govorov and N.A. Nikolaeva, *Izv. Akad. Nauk. SSSR. Ser, Khim*, **9** (1976), 1820; *Chem. Abst.*, **86** (1977), 16722 y.
5. B.M. Mikhailov, G.S. Ter – sarkisyan and N.N. Govorov, *Izv. Akad. Nauk. SSSR. Ser. Khim*, **8** (1976), 1823; Chem. Abst., **86** (1977), 16723 z.
6. C. Summerford and K.Wade, *J.Chem. Soc.*, A (1970), 2010.
7. B. Samuel, R. Smith, C.Summerford and K.Wade, *J.Chem. Soc.*, A (1970), 2016
8. M. Das and S.E. Livingstone, *Inorg Chim. Acta*, **19** (1976), 8.
9. K. Singh, R.V.Singh and J.P. Tandon, *Polyhedron*, 7 (1988), 151.
10. H. Jadamus, Q. Fernando and H. Freiser, *J. Am. Chem. Soc.*, **86** (1964), 3056.
11. A. Pasini and M. Guttoti, *J. Coord. Chem.*, **3** (1974), 379.
12. R.V.Singh and J.P. Tandon, Synth. *React. Inorg. Met.-Org.Chem.* **11**, (1981), 109.
13. R.K. Sharma, R.V. Singh and J.P. Tandon. *J. Inorg Nucl. Chem.*, **42** (1980), 1267.
14. C. Saxena and R.V.Singh, *Main Group. Met. Chem.*, **15** (1992), 31
15. V.P. Singh, R.V. Singh and J.P. Tandon, *J.Inorg. Biochem.*, **39** (1990), 237.
16. V.P. Singh, R.V.Singh and J.P. Tandon, *Synth. React., Inorg. Met.-Org. Chem.* **19**, (1989), 669.
17. T. Pandey, V.P.Singh and R.V.Singh, *Main Group Met. Chem.*, **21**(1998), 185
18. L.H. Thoman, *J. Chem. Soc.*, (1946), 820.
19. E.R. Rawlins, *"Bentray's Text book of Pharmaceuticals", 8th ed., Boilliere Tindall, London* (1977).

Received: August 24, 1998 - Accepted: September 30, 1998 - Accepted in revised camera-ready format: February 16, 1999